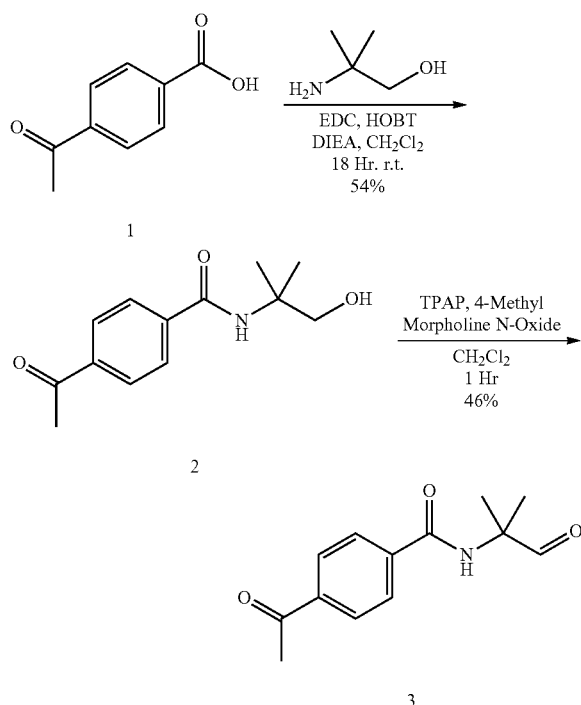


Example 16

[0517]

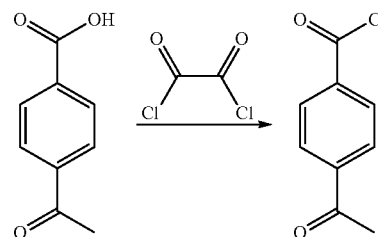


A mixture of 2-amino-2-methyl-1-propanol (4 mL, 42 mmol), CH_2Cl_2 (200 mL), 4-acetyl benzoic acid (1, 6.9 g, 42 mmol), EDC (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl , 12.1 g, 63 mmol), HOBT (N-hydroxybenzotriazole H_2O , 6.4 g, 42 mmol), and Hunig's base (diisopropylethylamine, 22 mL, 126 mmol) was stirred at room temperature for 18 hours. Upon completion (TLC, LC/MS) the reaction mixture was concentrated, and the resulting residue was diluted with EtOAc (50 mL) and washed with NaHCO_3 (2x40 mL) and brine (40 mL). The organic layer was dried (MgSO_4), filtered, and the filtrate was concentrated. The crude material was purified by flash column chromatography (4:1:1 hexanes:EtOAc: CH_2Cl_2 ; 1:1:1 hexanes:EtOAc: CH_2Cl_2 ; 1:1 EtOAc: CH_2Cl_2) to remove bisacylated material. Alcohol 2 was obtained in 54% yield (5.36 g).

Tetrapropylammonium perruthenate (TPAP, 387 mg, 1.1 mmol) was added portion-wise to a solution of 2 (5.36 g, 22.8 mmol), CH_2Cl_2 (46 mL, 2 mL/mmol), 4-methyl-morpholine N-oxide (4 g, 34.2 mmol), and molecular sieves, 4 Å activated powder (11.4 g, 500 mg/mmol) at 0° C. under N_2 . The reaction was allowed to warm to r.t. after 15 minutes. After 1 hour the reaction was complete (TLC) and was filtered through silica, which was eluted with EtOAc (100 mL), and the filtrate was concentrated. This yielded 4.4 g of light pink solid (3). The material was recrystallized: 1:1 Hexanes:EtOAc (5 mL), CH_2Cl_2 (20 mL), and MeOH (10 mL) were added portion-wise with heating and sonication. This was brought to a boil after which hexane (100 mL) was added while cooling. Crystals immediately began to precipitate as the solution was cooled. The mixture was filtered and the crystals were washed with hexane (10 mL), affording 2.46 g (46%) of 3 as off-white fluffy crystals.

Example 17

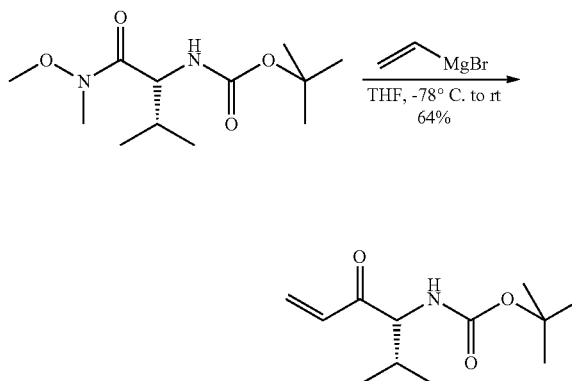
[0518]



[0519] A solution of 4-acetyl benzoic acid (500 mg) in oxalyl chloride (5 mL) was heated to reflux for 2 hours. Any remaining oxalyl chloride was evaporated by rot-vap, and the residue was dried by vacuum. The yield of product was quantitative.

Example 18

[0520]



((R)-1-Isopropyl-2-oxo-but-3-enyl)-carbamoyl-methyl-propyl ester

[0521] Tetrahydrofuran (THF, 100 mL) and a 1.0M solution of vinyl magnesium bromide in THF (360 mL, 360 mmol, 3.1 equiv) was cooled to -78° C. while stirring under a nitrogen atmosphere. The mixture was treated dropwise with a solution of [(R)-(methoxy-methyl-carbamoyl)-methyl-propyl]-carbamoyl-methyl-propyl ester (30.3 g, 116 mmol, 1 equiv) in THF (50 mL) over 30 min. After the resultant dark yellow mixture was stirred for 30 min at -78° C., the cooling bath was removed and the reaction mixture was warmed slowly to room temperature overnight (15 h). The reaction mixture was poured slowly into an ice-chilled solution of 1N aqueous hydrochloric acid (700 mL) and then warmed to room temperature. The organics were extracted with (3x600 mL) ethyl acetate, dried over sodium sulfate, filtered, and concentrated in vacuo. Purification by flash column chromatography (5-10% ethyl acetate/hexanes) provided the product as a white solid (16.8 g, 64%). ESMS $[\text{M}+\text{H}]^+$: 228.4.